

REMARKS

Reconsideration of the above referenced application is respectfully requested.

Upon entry of the foregoing amendment, Claims 1-11, 13-14, 16-45, 47-51, 58-59 and 63 are presently pending. Claims 1, 23, 40 and 59 have been amended. Basis for the amendments and new claims may be found throughout the specification, in the figures (i.e., Figure 8) and in the claims as originally filed. Claims 12, 46, 52-57, 60-62 and 64-83 have been cancelled herein without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the cancelled claims in one or more continuation or divisional application. No new matter has been introduced and entry of the amendment is requested.

Claim Objections

Claims 23, 24, 26, 33, 35, 37 and 59 stands objected to for recitation of abbreviations as set forth on page 2 of the Office Action. Applicants submit that one of skill in the art would be able to readily identify the subject matter of the various abbreviations in the claims based on the disclosure in the specification and publicly available information, as follows:

Claim 23 recites flt3 which is a cytokine included in the examples of other therapeutic genes of interest described in paragraph [0116] of the specification.

Claim 24 recites examples of other therapeutic genes of interest described in paragraph [0116] of the specification which include chemokines such as MIP, CCR7 ligand and proteins that stimulate interactions with immune cells such as B7 and TAPs.

Claim 26 recites further examples of other therapeutic genes of interest described in paragraph [0116] of the specification which include tumor-associated antigens including immunogenic sequences from MART-1, gp100 (pmel-17), MAGE, BAGE, GAGE, NY-ESO-1, MUM-1, KIA 0205, HLA-A2R1701, G-250, MUC-1 and LDLR-FUT.

Claim 33 recites TrpRS which is an anti-angiogenic gene described in paragraph [0116] of the specification.

Claim 35 recites still further examples of therapeutic genes of interest described in paragraph [0116] of the specification such as growth factor/cytokine inhibitors which include sFlk, sNRP1, the angiopoietin/tie antagonist, sTie-2, chemokines (IP-10, PF-4, Gro-beta, IFN-gamma (Mig), Ephrin/Eph antagonist such as sEphB4 and anti-angiogenic genes such as METH-1, and METH-2.

Claim 37 recites examples of suicide genes, which are described in paragraph [0117] of the specification, including genes that encode for carboxypeptidase G2 (CPG2), carboxylesterase (CA), cytosine deaminase (CD), nitroreductase (NR), purine nucleoside phosphorylase (PNP), thymidine phosphorylase (TP), varicella zoster virus thymidine kinase (VZV-TK).

Claim 59 recites RID, an E3 protein which is described in paragraph [0301] of the specification which makes reference to the E3 regions reviewed in Wold, et al., E3 transcription unit of adenovirus. in "The Molecular Repertoire of Adenoviruses I," ed. by W Doerfler and P Bohm, pp 237-274, Springer-Verlag, Berlin. 1995.

Claims 23 and 74 stand objected to for the presence of extra periods within the claim. Claim 74 has been cancelled and Claim 23 has been amended obviating the basis for objection.

Rejection under 35 U.S.C. §112, second paragraph.

Claims 1-11, 13-14, 16-45, 47-51, 58-59, 62-64 and 67-83 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reasons stated on pages 3-4 of the Office Action.

The claims have been amended to recite “in sequential order in the 5’ to 3’ direction” in order to clarify that the “sequential order is from the 5’(or left) end of the vector beginning at the ITR and extending to the 3’(or right) ITR.

Claim 7 has been amended to remove the word “further”, thereby clarifying that the claimed vector has a single deletion.

Applicants respectfully submit that the grounds for the rejection have been obviated by the amendments submitted in this communication. Withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 1, 3-6, 8, 9, 14, 16, 18-25, 29, 35-38, 48, 58, 59, 62, 67, 69-76, 78, 82 and 83 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Johnson et al., US Patent Publication No. 2004/0151696. Applicants respectfully submit that the presently claimed invention is not anticipated by Johnson et al.

Johnson et al. is cited as disclosing oncolytic vectors and particles that comprise a left ITR, termination signals such as those associated with the E1A or E2 genes or inserted transgenes, a human E2F-1 promoter driving expression of E1a or E4, a right ITR and a packaging signal (Fig 4, Ex. 1 and Paragraph 60).

Anticipation under 35 U.S.C. § 102 requires that the reference “must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present.” (MPEP §706.02). “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Johnson et al. disclose a replication deficient adenoviral vector system that can be used in gene transfer. Further, Johnson et al. disclose termination signals such as those associated with the E1A or E2 genes or inserted transgenes. Johnson et al. does not disclose a recombinant oncolytic adenoviral vector comprising in sequential order in the 5’ to 3’ direction: a left ITR, a termination signal sequence that is isolated from its genetic source and inserted into the viral vector at a suitable position upstream of a E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector-and a right ITR.

Hence anticipation does not lie and the rejection should be withdrawn.

Rejection under 35 U.S.C. §103(a).

Claims 1-9, 14, 16, 18-25, 29, 35-38, 40, 41, 43, 48, 58, 59, 62, 63, 64, 67, 69-76, 78, 82 and 83 stand rejected under 35 USC § 103(a), as allegedly obvious over Johnson et

al., US Patent Publication No. 2004/0151696 in view of George and Blazing (5880102), as evidenced by Haring and Shenk (Cell, 1983, pages 695-703).

Johnson et al. is described above.

On page 7 of the Office Action, George and Blazing (5880102), are cited as teaching an adenovirus vector; Ad:Pac-Bgal which has an E1a enhancer, with an SV40 poly A sequence 5' to the left ITR and 3' to the E1A gene and a packaging signal inserted at the 3' end of the vector. The Office Action refers to Fig. 47 and col. 2, line 6-10 of George and Blazing.

George and Blazing teach plasmids devoid of adenoviral E1a enhancer and packaging signal sequences that are replicable and selectable in bacteria, and which comprise an adenoviral terminal repeat, a promoter/multiple cloning site (MCS)/poly A and intron unit, and an adenoviral recombination sequence (that is, a sequence that overlaps with restricted virus that is sufficient in length for recombination), wherein the terminal repeat is located 5' to the promoter/MCS/poly A (column 2, lines 12-19).

The vector systems taught by George and Blazing are replication deficient (column 2, lines 4-5) and do not teach or suggest an oncolytic vector which contains a termination signal sequence that is isolated from its genetic source and inserted into the viral vector at a suitable position 3' to the left ITR and upstream of a gene essential for replication.

Haring and Shenk (Cell, 1983, pages 695-703, abstract) is cited as teaching an adenovirus vector; with deletion of an element with enhancer properties located between -141 and -305 relative to the E1A cap site at +1.

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all of the claim limitations. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991) and MPEP § 2142. Moreover, when applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to: (A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) Reasonable expectation of success is the standard with which obviousness is determined. Hodosh v. Block Drug Co., Inc., 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

On page 7, the Office Action concludes that it would have been obvious to one of ordinary skill in the art at the time the instant application was filed to have combined the oncolytic vectors and particles allegedly taught by Johnson et al. as including a left ITR, termination signals such as those associated with the E1A or E2 genes or inserted transgenes, a human E2F-1 promoter driving expression of E1a or E4, a right ITR and a packaging signal together with an adenovirus vector in which the SV40 poly A sequence is 5' to the left ITR and 3' to the E1A gene where nucleotides 103-551 are deleted as taught by Hearing and Shenk to arrive at the claimed subject matter.

As set forth above, Johnson et al. disclose replication deficient adenoviral vector system that can be used in gene transfer, not oncolytic vectors, as presently claimed. Further, Johnson et al. disclose termination signals such as those associated with the E1A or E2 genes or inserted transgenes, not a termination signal sequence isolated from its genetic source and inserted into the viral vector, as presently claimed.

George and Blazing, directed to plasmids devoid of adenoviral E1a enhancer and packaging signal sequences that are replicable and selectable in bacteria and which contain an intron unit which comprises a promoter/multiple cloning site (MCS)/poly A does not cure the deficiencies of Johnson et al. Similarly, Hearing and Shenk, cited as teaching deletion of a particular E1A enhancer sequence of Ad5 does not cure the deficiencies of Johnson et al. or George and Blazing, alone or in combination.

It follows that a combination of the cited references does not teach or suggest all of the features of Claim 1 which encompasses a recombinant oncolytic adenoviral vector comprising in sequential order in the 5' to 3' direction: a left ITR, a termination signal sequence isolated from its genetic source and inserted into the viral vector, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector-and a right ITR or Claim 40 which has the additional feature of an adenoviral packaging signal 3' to a human E2F-1 promoter operably linked to the E1A gene, and 5' to a right ITR, and claims dependent thereon.

Therefore, a *prima facie* case of obviousness has not been established and the rejection should be withdrawn.

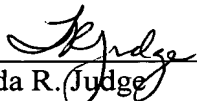
Conclusion

In light of the above, Applicants submit that this application is now in condition for allowance and therefore request favorable consideration. If any issues remain which the Examiner feels may be best resolved through a personal or telephonic interview, the

Examiner is respectfully requested to contact Applicants' counsel, Linda R. Judge at
(415) 836-2586.

Respectfully submitted,

DLA PIPER RUDNICK GRAY CARY U.S. LLP



Linda R. Judge
Registration No. 42,702

1200 Nineteenth Street, N.W.
Washington, D.C. 20036-2412
Telephone No. (202) 861-3900
Facsimile No. (202) 223-2085